DEPARTMENT OF HEALTH & HUMAN SERVICES

93404

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone: 313-226-6260

WARNING LETTER
2002-DT-30

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

July 9, 2002

Edward A. Kling
President
D.S.C. Products, Inc.
1979 Latimer Drive
Muskegon, Michigan 49442

Dear Mr. Kling:

A May 20 through June 11, 2002 limited inspection of your firm's drug manufacturing operations found that your firm is operating in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act). During the inspection, our investigators documented numerous significant deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211), which cause your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the Act.

Please refer to the list of inspectional observations which was issued at the conclusion of the inspection (copy enclosed) for additional details:

1) Failure to have a quality control unit adequate to perform its functions and responsibilities, as required by 21 CFR 211.22, as demonstrated by the number and type of inspectional observations.

2) Failure to ensure that the cleaning methods used to clean equipment and utensils are adequate to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond established requirements, as required by 21 CFR 211.67. For example, see FDA 483 observation 15.

3) Failure to adequately examine and test components, containers, and closures to determine conformance to established standards and acceptance for use, as required by 21 CFR 211.84(d). For example:

   a) Representative samples of each shipment of each lot are not collected for testing or examination, and raw material sample compositing is not an acceptable practice (FDA 483 observations 10 and 11).

   b) The reliability of supplier reports of analysis has not been appropriately validation at appropriate intervals (FDA 483 observation 9).

4) Failure to have adequately designed written procedures for production and process control to assure that drug products have the identity, strength, quality, and purity they purport or are represented to possess, as required by 21 CFR 211.100. For example:

   a) Written procedures do not define how process validation will be conducted or documented (FDA 483 observation 21).

   b) No written validation plan or written validation protocols were available at the time of the inspection (FDA 483 observation 22).

   c) Retrospective validation reports available at the time of the inspection do not reference the predetermined acceptance criteria, do not evaluate intra-run variability, and appear to be based on lots produced with inadequate laboratory and production controls (FDA 483 observations 23 and 24).

5) Failure to calculate actual yields and percentages of theoretical yield at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the drug product as required by 21 CFR 211.103. For example, see FDA 483 observation 16.

6) Failure to establish and follow validated sampling and testing procedures of in-process materials and drug products to assure batch uniformity and integrity of drug products, as required by 21 CFR 211.110. For example, see FDA 483 observations 17 and 18.

7) Failure to establish and follow written procedures prescribing a system for reprocessing batches that do not conform to standards or specifications, as required by 21 CFR 211.115(a). For example, see FDA 483 observation 20.

8) Failure to have the quality control unit review and approve reprocessing activities, as required by 21 CFR 211.115(b). See FDA 483 observation 19.

9) Failure to have changes in any specifications, sampling plans, test procedures, or other laboratory control mechanisms reviewed and approved by the quality control unit prior to implementation, as required by 211.160(a). For example, see FDA 483 observation 3.

10) Failure to assure that laboratory controls include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity, as required by 21 CFR 211.160(b). For example:

   a) There is no data available to establish that analytical methods used to assay finished products meet appropriate standards for accuracy and reliability (FDA 483 observation 1).

   b) There is no data available to establish the purity of the reference standards used to assay finished products (FDA 483 observation 2).

   c) The calibration of analytical instruments is not being conducted in accordance with you established written program (FDA 483 observation 4).

   d) All [redacted] methods do not include a system suitability test to insure that the system is operating properly (FDA 483 observation 6).

   e) Volumetric glassware is not always used to take volume measurements during assays of active ingredients in drug products (FDA 483 observation 7).

   f) Scientifically sound and appropriate sampling plans have not been established or used (FDA 483 observation 10).

11) Failure to establish and document the accuracy, sensitivity, and reproducibility of test methods employed, as required by 21 CFR 211.165(e). For example:

a) Data is not available to establish that the analytical methods used to assay finished products meet proper standards of accuracy and reliability as applied to the product tested (FDA 483 observation 1).

b) Data is not available to support the purity of some reference standards used to assay finished products (FDA 483 observation 2).

12) Failure to assure that the acceptance criteria for the sampling and testing conducted by the quality control unit is adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release, as required by 21 CFR 211.165(d). For example, see FDA 483 observation 8.

13) Failure to assure that the written testing program is designed to assess the stability characteristics of drug products, as required by 21 CFR 211.166. For example, no data is available to show that the analytical methodologies used in performing stability tests are stability indicating (see FDA 483 observation 5).

14) Failure to conduct annual product reviews in accordance with written procedures, as required by 21 CFR 211.180(e). For example, see FDA 483 observation 12.

15) Failure to maintain complete records of any modification of an established method employed in testing, including the reason for the modification and data to verify that the modification produced results at least as accurate and reliable for the material being tested as the established method, as required by 21 CFR 211.194(b). For example, see FDA 483 observation 3.

16) Failure to maintain complete records of all stability testing performed, as required by 21 CFR 211.194(e). For example, see FDA 483 observation 13.

The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Good Manufacturing Practice Regulations. Other Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

We request that you take prompt action to correct these deviations and to ensure that your drug manufacturing systems are in full compliance with the Act and regulations promulgated thereunder. Failure to make prompt corrections may result in regulatory action without further informal notice, such as seizure and/or injunction.

We note that compliance commitments were made by you following the issuance of warning letter 95-DT-13 on March 3, 1995, and that you have not lived up to these commitments. We acknowledge receipt of your June 21, 2002 written response to the list of inspectional observations. While you commit to take specific steps to correct the noted violations, your proposed actions will not result in compliance with the regulations. We also note that no commitments are made to correct the systemic weaknesses that allowed these violations to occur in the first place, to assure that similar violations will not recur, or to review those aspects of your operations not covered during our inspection.

Because of the significance and extensive nature of the above violations, we request that you and your advisors contact us, within five (5) working days of your receipt of this letter, to arrange a meeting at our Detroit offices to discuss this matter in person. Please be prepared to discuss the status of all products manufactured by your firm that are currently in distribution channels and to discuss what actions you are prepared to take to bring your firm into compliance. Please contact Compliance Officer Sandra Williams at 313-226-6260, extension 134, to schedule this meeting.

Sincerely yours,

John P. Dempster

for Joann M. Givens
District Director
Detroit District

Enclosures: FDA 483 for 5-20/6-11-02 inspection